

JUL 02 2007

To Eric Olson PTO to facilitate conversation for allowance July2-07 from Peter Migaly 10/627,358 Total of 3 pages Faxed to (571) 273-9051

Figure 1.: Examples of how the PTO examiner lines of reasoning is not convincing as it skips steps that would lead a third party (clinician) to consequent faulty logic. The PTO is not thinking as the skilled in the art has to. (The PTO is leaving out the risk/benefit/alternative analysis that would lead the clinician to commit malpractice. We have stated that in our reply! Yet the PTO skips that and repeats that his "logic" would be logical to the clinician, and that the clinician (without our guidance and enablement) would had no problem of following the PTO's line of reasoning (and skipping steps) and come to the same conclusions as the teaching of our invention and claims: (In doing so the non-clinicians would be charged or imprisoned for practicing medicine/psychiatry without license, and the clinicians would loose malpractice cases of not doing the risk/benefit/alternative analysis, and being negligent!)

- Example of the illogical faulty thinking by the PTO examiner:

Rapid onset of combination drugs: if A is as rapid as A+B, and A+B has no proven or explained benefit over A alone but B has potential lethal side effect; and in addition there is C that is an antidepressant monotherapy that is even faster acting then A, or A+B then the

PTO states (that would lead any clinician to commit malpractice) that:

A+B -----(PTO skipping steps)-----> use it (A+B)

(that is the PTO states that the average clinician would chose to commit malpractice and skip the required steps, and use this as initial Rx, and for non-TRD and non-psychotic depression without guidance and reasons, that is without enablement)

(PTO further errs on several other things, that is Tollefson never made the conclusion that the PTO stated would be logical to the skilled in the art, but in fact it is only the reasoning of the PTO, and only if the PTO disregards our teaching - that they did.)

- Instead the clinician is obligated to think differently:

(using drug A+B)

Step one:

A+B → use risk/benefit/alternative analysis →

(if A is as rapid as A+B and B has even life threatening side effect then there is no benefit to use A+B over A.

Therefore by doing this analysis the clinician is not permitted to use the combination (unless other info or guidance was disclosed by Tollefson, (but it was not the case).

End result

→ for the skilled in the art

do not use it (A+B); it leads to malpractice!

(Do not use A+B for initial Rx for non-TRD non-psychotic depression)

Step two:

If there is C that is an antidepressant monotherapy that is even faster acting then A, or A+B and C does not have B compound's potentially lethal side effect and is generally accepted as safer than A+B then

End result

→ for the skilled in the art

do not use it (A+B); it leads to malpractice!

(Do not use A+B for initial Rx for non-TRD non-psychotic depression)

Step three; another step: the clinician should also compare his decision to the current standard of care (including teachings against our inventions that we have included in our 1st reply).

End result

→ for the skilled in the art

do not use it (A+B); it leads to malpractice!

(Do not use A+B for initial Rx for non-TRD non-psychotic depression)

Presented secondary factors also supported this, but again the PTO examiners disregarded that too in order to maintain their unconvincing line of reasoning. With that the PTO denies our claims and builds up to other erroneous conclusions.

On the other hand we have provided enablement to overcome these barriers, and this was presented in our application and claims.

To Eric Olson PTO to facilitate conversation for allowance July2-07 from Peter Migaly 10/627,358 Total of 3 pages Faxed to (571) 273-9051

Figure 2.: Examples of how the PTO skips steps with unconvincing line of reasoning and is not thinking as the skilled in the art has to. **PTO states (that would lead any clinician to commit malpractice) that:** Faour (in describing a delivery method), Chappell, Tollefson, or as we add to this list now, Nesbitt and Pharmacia & Upjohn company's WO 02/053140 A2; (or any other prior art that was brought to our attention up to date), or the artisan would have followed the PTO's reasoning:

A+B is used:

- for the wide definition of depression (therefore the PTO states the non-TRD and non-psychotic depression should be understood in that term against the current practice of the standard of care, and despite the fact that the cited prior art was not disclosing of why and for what benefit A+B should be used at all or specifically as initial treatment for these subcategories i.e. the non-TRD and non-psychotic depression, (therefore the PTO is skipping clinical decision making steps), or
- for more broader mental illnesses (including depression – “– [ditto all italics from above]), or
- for an even broader term, that is for all of DSM diagnosis, for all of mental illnesses (that the WO 02/053140 A2 have explicitly incorporated as reference) (“–[ditto all italics from above])

“therefore – as per the PTO - the skilled artisan would had no problem in applying the method for non-TRD and non-psychotic depression as initial Rx”

PTO's end result ----- (PTO skipping steps) ----- → use it

(that is the PTO states that the average clinician would chose to commit malpractice and skip the required steps, and use this as initial Rx, and for non-TRD and non-psychotic depression without guidance and reasons, that is without adequate enablement)

- **Instead the clinician is obligated to think differently (using drug A+B):**

Step one:

A+B → where is the disclosure that why that should be used also for non-TRD and non-psychotic depression?

There is none! ----- **End result----- → for the skilled in the art
do not use it; it leads to malpractice!**

Step two:

A+B → what benefit does A+B provide over known risks that warns against using it?

Was there an adequate disclosure and enablement?

There is none! ----- **End result----- → for the skilled in the art
do not use it; it leads to malpractice!**

Step three:

A+B → why should that be used as an initial Rx?

Was there an adequate disclosure and enablement?

There is none! ----- **End result----- → for the skilled in the art
do not use it; it leads to malpractice!**

Step four:

A+B → what benefit does A+B provide over known risks that warns against using it as an initial Rx? Was there an adequate disclosure and enablement?

There is none! ----- **End result----- → for the skilled in the art
do not use it; it leads to malpractice!**

Step five:

A+B → compare the use of A+B for non-TRD and non-psychotic depression as an initial Rx to the current standard of care and recommendations including teaching against its use and use the risk/benefit alternative analysis (and see if there was an adequate disclosure and enablement in the cited prior art in this regard).

There is none! ----- **End result----- → for the skilled in the art
do not use it; it leads to malpractice!**

Therefore by doing this analysis the clinician is not permitted to use combination for non-TRD and non-psychotic depression as an initial Rx (unless guidance was disclosed with adequate enablement by the cited prior art. (but that was not the case for any of the cited prior arts!))

Presented secondary factors also supported this, but again the PTO examiners disregarded that too in order to maintain their unconvincing line of reasoning. With that the PTO denies our claims and builds up to other erroneous conclusions. On the other hand we have provided enablement to overcome these barriers, and this was presented in our application and claims.

To Eric Olson PTO to facilitate conversation for allowance July2-07 from Peter Migaly 10/627,358 Total of 3 pages Faxed to (571) 273-9051

Figure 3.: Graphical example #3 of the unconvincing line of reasoning by the examiner, of not understanding the importance of "substantially all of said patients" (within the group of patients described in independent claims 1, 2; that is within non-TRD, and non-psychotic depression). The examiner also misinterprets the term "benefit of the group":

PTO: In Figure 1 and Figure 2 we had shown of why the PTO's logic to use A+B couldn't be followed by the clinicians without the artisan committing malpractice. So at the time of our invention – as strong secondary factors also show – the clinicians had to follow the steps below not only for the individual patients but even more for "substantially all of said patients" or "all patients" within the non-TRD and non-psychotic depression and in particular if it is for initial treatment:

A+B as initial Rx for "substantially all" or "all patients" (within the claim 1, and 2, that is for non-treatment resistant, non-psychotic patients) -----→ **(Clinicians at the time of our invention and in doing the required steps of Figure 1 and Figure 2,)**

End result-----→ **do not use it (A+B)**

However, also as the secondary factors show the clinicians were still skipping steps like the "benefit of the group analysis" that we have shown being an important and crucial step that drastically changes the clinical decision for the benefit of the group and the individual, and thus changes the standard of care and first choice of treatment.

versus (see also Guidance 2a) and b) in our reply to the first office action, specification re-entered from the provisional application)

My invention and teaching is recognizing and is adding additional steps:

A+B as initial Rx for substantially all or all patients (within the claim 1,2, that is for non-treatment resistant, non-psychotic patients for the benefit of the group) --→ **(black box with additional steps)** -----→ **do use A+B**

The group of substantially all or all patients (within the claim 1,2, that is for non-treatment resistant, non-psychotic patients) and as for initial treatment with A+B:

Step one:

We do not know that who in the group would be suicidal, therefore another risk/benefit/alternative analysis should be performed: The analysis is on the risk of giving the medication combination versus not giving it. We need to ask:

When would more death occur?

Since we do not know who in the group would be affected therefore the benefit of the group is also for the benefit of the individual. -----→ **do use A+B**

(The analysis is similar to our appendicitis risk benefit analysis that is known to the art and what we have specifically described in our provisional application).

Step two:

Compare this decision to other practices within the standard of care:

Compare the Suicide risk of MDD to the actual suicide risk of Borderline personality disorder (BPD), where the same combination is given and where it is an accepted method within the standard of care. [see Guidance 2b) in our reply to the first office action] Since the completed suicide rate is significantly higher in MDD than in BPD and since other enablement (reasons) were given, the justification to use A+B is clinically there with absolute clarity. -----→ **do use A+B**